

## **ABSTRACT**

The present invention relates to identification of tumor suppressor activity of a protein, caspase-8 (CASP8), and to related diagnostic and therapeutic compositions and methods. The discovery of this tumor suppressor activity provides screening targets as well, particularly screening for compounds that overcome gene inactivation that results from genomic methylation of the promoter. In particular, *CASP8* is functionally inactivated in greater than 90% of all *MYCN* amplified neuroblastoma cell lines analyzed. Inactivation of *CASP8* was observed to occur by homozygous deletion, heterozygous deletion coupled with gene silencing by methylation, and homozygous gene silencing by methylation. A PCR methylation analysis for inactivation of *CASP8* is described.